Remarks

The Rejection of Claims 21-47 Under 35 U.S.C. § 112, paragraph 2

Claims 21-47 are rejected as indefinite for failing to recite the sequence of INGAP. This rejection is respectfully traversed.

The Office Action urges that without a sequence there is no way to determine the structure or function of INGAP. However, as of the effective filing date of this application (October 30, 1996) INGAP was known in the art. On August 29, 1996, PCT Application No. US96/01528 published as WO 96/26215, disclosing the nucleotide and amino acid sequences of INGAP. On October 7, 1996 Genbank published the nucleotide and amino acid sequences of INGAP. Thus the structure of INGAP was known in the art. PCT application US 96/01528 also discloses the function of INGAP as a stimulator of pancreatic ductal cell proliferation. Thus the term INGAP had meaning in the art and identifies a protein with a known structure and function and its encoding gene.

Claims 22 and 28 recite particular amplification primer sequences. These claims do not require any more structural definition, as use of the recited primers does not require knowledge of the INGAP sequence. Thus these claims should not be subject to this rejection even if, *arguendo*, the rejection were proper with regard to the other claims.

Because INGAP was known in the prior art and had a known structure (and function) associated with it, the claims do not require definition by recitation of a sequence identifier.

Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 21, 23, 24-47 under 35 U.S.C. § 112, paragraph 1

Claims 21, 23, 24-47 are rejected as broader than the enablement provided by the specification. The rejection urges that only expression constructs using SEQ ID NO: 6 are enabled.

Preliminarily, claim 28 defines the coding sequence for mature human INGAP as the product of amplification with two defined primers. Thus claim 28 is not subject to the alleged infirmity, as use of these two primers produces an INGAP coding sequence. Thus this claim is enabled, similar to claim 22 which the Office Action acknowledges is enabled.

The Office Action asserts that INGAP is a novel protein and thus the "assistance from the prior art" cannot be relied upon for practice of the invention. However, as discussed above, INGAP was in the prior art at the time of filing the subject application and its parent. The discovery of the present inventors is not the INGAP protein *per se,* but rather the positive and unexpected effect that deletion of the signal sequence has on expression of INGAP. One of skill in the art could readily utilize INGAP as disclosed in the subject application, or as available in the literature or in GenBank. Any such INGAP coding sequence could be used. Those of skill in the art would know how to use allelic variants as well. The invention requires the deletion of the signal sequence. The signal sequence is disclosed in the subject application. It is specified by sequence identifier in claims 29 and 45 and their dependents. Because INGAP was part of the state of the art, those of ordinary skill would be able to use INGAP and its obvious variants, including allelic or species variants, if any. Those of ordinary skill in the art could readily make

and use the invention for any INGAP, as it was in the state of the art, and would not require undue experimentation.

Wands factors provide a framework for analysis of relevant facts for determining enablement. The factors to consider are:

1. the quantity of experimentation necessary
2. the amount of direction or guidance presented
3. the presence or absence of working examples
4. the nature of the invention
5. the state of the prior art
6. relative skill of those in the art
7. the predictability or unpredictability of the art
8. the breadth of the claims

Wands factors weigh in favor of the enablement of the rejected claims. INGAP was known in the art of molecular biology. (Factor 5.) Molecular biologists generally have Ph.D.s plus several years of post-doctoral training. (Factor 6.) Working examples are provided. (Factor 3.) The specification teaches how to isolate INGAP proteins. The specification provides INGAP coding sequence which can be used to fish out other INGAP coding sequences from other individuals or other mammals. (Factor 2.) The art knows how to identify signal sequences and termination codons using sequence features alone. (Factor 7.) The specification teaches the biological function of INGAP as stimulating pancreatic ductal cell proliferation. (Factor 2.) Thus, very little experimentation would be required to practice the invention with any INGAP protein.

(Factor 1.) The claims are narrow, claiming only an improvement over the prior art to obtain higher expression levels by deleting the signal sequence. (Factor 8.) Weighing these factors, one is led to conclude that the claims are indeed enabled.

The Office Action at page 3, paragraph 3 through page 4, paragraph 1, appears to pertain not to the subject application, but to a different application unknown to applicants. SEQ ID NOS: 4 and 6 are said to be the only polynucleotides taught in the specification. In fact claim 6 is not a nucleotide sequence at all, and SEQ ID NOS: 1, 2, and 3 are also disclose nucleotide sequences. The specification is said not to provide structural or functional parameters or features that polypeptides must retain to allow one to identify them as OFQ receptors (*sic*). Indeed, the specification does provide structural and functional features. INGAP protein is disclosed as a ductal cell proliferation stimulator. This function is localized to amino acids 103 to 122, as disclosed in parent applications 08/401,530 and 08/709,662, which were expressly incorporated into the subject application. Thus, Applicants teach that any molecule with this function which resides in the core region of just 20 amino acids is an INGAP protein. This provides extremely good structural and functional guidance.

Contrary to the assertion at the bottom of page 3 of the Office Action, these are <u>not</u> novel proteins. The quotation cited by the Office Action as being from page 2, last sentence of the subject specification does not appear to derive from the subject application, but from an application unknown to Applicants. INGAP protein was in the prior art relative to the subject application. Contrary to the Patent and Trademark Office's assertion of novelty for INGAP, the prior art taught both a common structure and functional feature to be used to identify INGAP

molecules. Thus, one of skill in the art could rely on both the prior art and the specification for guidance to enable the full breadth of the claims.

Withdrawal of this rejection is requested as the claims are enabled by the specification in view of the state of the art.

Recapture

The Office Action asserts that claims 21, 23, and 24-47 are prohibited to Applicants because they attempt to broaden the scope of the patent claims back to the original scope which had been relinquished in the parent (08/741,096) of the continuation-in-part application (08/909,725) which issued into U.S. Patent 5,804,421.

Claims 21-22, directed to primers, do not correspond to any claims in either the parent ('096) or the CIP ('725). No claims were originally presented to primers. Thus claims 21-22 are not implicated by the recapture rule as no claims of this scope and subject matter were ever relinquished.

Similarly claims 23-28, directed to methods of making an expression construct, do not correspond in subject matter to any originally presented claims in the '096 or '725. Thus those claims cannot run afoul of the recapture rule as such claims were not relinquished.

Claims 29-44 are directed to recombinant constructs. Claims 45-46 are directed to a method of producing INGAP from recombinant host cells. And claim 47 is directed to recombinant host cells *per se*. While these claims do correspond to the general subject matter of claims originally presented in the '096 and/or '725, they do not attempt to broaden back to the original scope. Claims in the '096 originally recited no sequence identifiers. They were

amended to recite sequence identifiers prior to abandonment of the '096. The '725 claims recited sequence identifiers as filed. Even if, *arguendo*, actions in the '096 pertain to the recapture of subject matter in this reissue application, claims 29-47 would not run afoul of the recapture rule. Claims 29-47 are not as broad as the scope of the original claims. Each of claims 29-47 recites "human INGAP." This limitation was not in the original claims of the '096. Thus claims 29-47 are intermediate in scope between the original claims of the '096 and the issued claims of the '725. Such scope is permissible under the reissue law.

"The recapture rule bars the patentee from acquiring, through reissue, claims that are the same or broader scope than those claims that were canceled from the original application." *In re Clement*, 45 USPQ2d 1161, 1165 (Fed. Cir. 1997) quoting *Ball Corp. v. United States*. "[A] reissue claim narrower in scope escapes the recapture rule entirely." *Id.* Since, the subject claims are narrower than the canceled (or original) claims, the recapture rule does not apply.

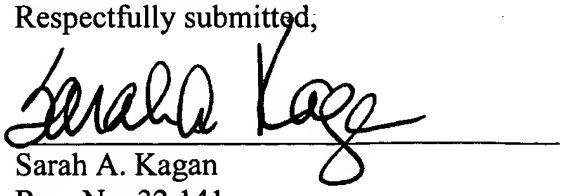
The MPEP discusses the reissue rule and the procedures to be used for determining whether a reissue application claim runs afoul of it.

> When a claim in a reissue application is in fact broadened, the examiner must next determine whether the broader aspects of that reissue claim relate to subject matter that applicant previously surrendered during the prosecution of the **original application (which became the patent to be reissued)**.

§ 1412.02 Emphasis added. The MPEP refers to an amendment made in the application which issued as a patent. The amendment which the Office Action points to occurred not in the application, but rather in an abandoned parent of a CIP. According to the MPEP, such an amendment is not relevant to recapture.

For all the reasons discussed, Applicants respectfully request withdrawal of the rejection under the recapture rule.

Respectfully submitted,



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MARKED-UP VERSION

48. (New) The method of claim 23 wherein the coding sequence for mature human INGAP encodes amino acids 27 to 175 as shown in SEQ ID No.: 6.

49. (New) The pair of oligonucleotide primers of claim 21 wherein the first of said oligonucleotide primers comprises 5'-GAAGAATCTCAAAAGAAACT-3' (nucleotides 12 to 31 of SEQ ID NO: 2 and the second of said oligonucleotide primers comprises 5'-TGCTCTTCCTGAGTGAA-TCC-3' (nucleotides 13 to 32 of SEQ ID NO.: 3).